

# Starch solutions in Australia: the empire strikes back

Rinaldo Bellomo

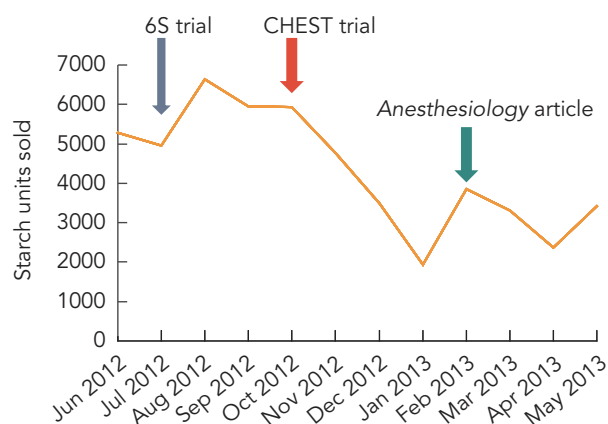
All who drink of this remedy will recover ... except those whom it does not help, who will die. Therefore, it is obvious that it fails only in incurable cases

— Galen

On 12 July 2012 in the *New England Journal of Medicine*, Scandinavian investigators led by Anders Perner reported the results of a double-blind, multicentre, randomised controlled trial (DB MC RCT) of hydroxyethyl starch (HES) in a balanced crystalloid solution versus the balanced crystalloid solution itself.<sup>1</sup> They found that patients who received HES had an increased risk of death and of acute kidney injury requiring treatment with renal replacement therapy. Did these findings affect the use of starch in Australia? Absolutely not (Figure 1).

About 3 months later, on 17 October 2012, the results of the Crystalloid Versus Hydroxyethyl Starch Trial (CHEST)<sup>4</sup> were published in the *New England Journal of Medicine*.<sup>2</sup> CHEST, also a DB MC RCT, confirmed that HES increased the incidence of acute kidney injury requiring renal replacement therapy. These findings, coming from Australia and New Zealand, led to a 19.5% decrease in sales of Voluven and Volulyte (the HES preparations marketed in Australia) in the following month, and a 67.4% decrease by January 2013 (Figure 1).

**Figure 1. Changes in sales of hydroxyethyl starch-containing fluid in Australia**



After publication of the Scandinavian (6S) trial,<sup>1</sup> there were no changes. Sales plummeted after the Crystalloid Versus Hydroxyethyl Starch Trial (CHEST) trial.<sup>2</sup> However, stability was restored after release of the *Anesthesiology* article.<sup>3</sup> (Data available from <http://www.imshealth.com/portal/site/imshealth> upon payment.)

This looked like a promising scenario for those “in a galaxy far, far away” who believe that practice should be based on high-level evidence. They were wrong. In an article published in *Anesthesiology* in early February this year, the other side focused on patients having surgery and on short-term physiological changes to demonstrate (in a warped logic that would have made Galen proud) that all was well with starch fluids, if they were only used in the operating theatres (a large area of starch sales).<sup>3</sup> Despite intense protests by various correspondents about the profound flaws of this analysis,<sup>5,6</sup> and concern because the four main authors reported conflicts of interest in relation to HES producers, it “worked”. HES sales in Australia in February 2013 doubled compared with January. They remained essentially stable until May 2013 (the last month for which data were available) — 3415 units (equivalent to about A\$40 000) were sold in May. Whether recent decisions by various regulatory authorities to restrict or remove HES from use<sup>7</sup> will prove successful remains to be seen. As reported by the *Financial Times*, it is likely that HES manufacturers will fight restrictions to the bitter end.<sup>8</sup> It makes one almost filled with admiration for Lilly, who pulled Xigris from the market the day after the results of the PROWESS-SHOCK trial were made public.<sup>9</sup> The lesson is clear: evidence is but a tiny part of the practice puzzle. When translating best evidence into practice is in conflict with the commercial interests of large and wealthy multinational companies, the game is much rougher than issuing guidelines or writing erudite reviews. It is much more like *Star Wars* than one could ever imagine. It remains to be seen whether the poorly armed and poorly resourced clinician–investigator with only the best interests of his or her patients at heart will, like the rebels, eventually win the war.

## Competing interests

None declared.

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